

Claims

What is claimed is:

1. A method for multi-dimensional imaging of a specimen region, comprising the steps of:
 - 5 a) acquiring images from a continuum of parallel focal planes, wherein each of the continuum of parallel focal planes is within a specimen region perpendicular to the incident light rays, such that a pseudo-projection is compiled; and
 - b) step a) is repeated for two or more viewpoints.
- 10 2. The method of claim 1 wherein step a) is repeated about an arc at least partially encircling the specimen region for tomographic image reconstruction.
3. The method of claim 1 wherein step a) is repeated about multiple arcs with common line or point of intersection at least partially encircling the specimen region for tomographic image reconstruction.
- 15 4. The method of claim 1, further comprising the step of using a computer algorithm to extract features of interest from one or more of the images.
5. The method of claim 1 further comprising the step of moving an optical element relatively to the specimen region to acquire the continuum of parallel focal planes.
6. The method of claim 5 wherein the optical element comprises an objective lens.
- 20 7. The method of claim 5 wherein the step of moving an optical element is accomplished by driving a piezoelectric element coupled to the optical element.
8. The method of claim 1, further comprising the step of imaging the continuum of parallel focal planes onto a two-dimensional array of detectors during a single integration period.
- 25 9. The method of claim 8, wherein the continuum of parallel focal planes is captured during a single integration interval of the two-dimensional array of detectors.
10. The method of claim 1, wherein the specimen region comprises a cell.
11. The method of claim 1, wherein the specimen region comprises an artificially generated test phantom.
- 30 12. The method of claim 1 wherein the step of acquiring images further includes the step of illuminating the specimen region with a laser.

13. The method of claim 1 wherein the step of acquiring images further includes the step of illuminating the specimen region with substantially incoherent light.
14. The method of claim 13 wherein the substantially incoherent light is generated by an arc lamp.
- 5 15. The method of claim 1 wherein the step of acquiring images comprises capturing images using at least one microlens array.
16. The method of claim 1, wherein the step of acquiring images comprises using a confocal arrangement with an extended lateral field of view.
17. The method of claim 1, wherein the step of acquiring images comprises the step of
10 moving an oil-immersion lens perpendicularly to acquire the continuum of parallel focal planes.
18. The method of claim 1, wherein the specimen region comprises a specimen within a specimen holder, wherein the specimen holder is selected from the group consisting of a micro-capillary tube, a plastic bead, polymer optical fiber, and a microscope slide.
- 15 19. The method of claim 1 wherein the step of acquiring images comprises capturing images using an array of collimator fibers wherein each fiber is mapped to a single pixel on a photosensor array.
20. The method of claim 19 wherein the photosensor array comprises a CCD array.
21. The method of claim 1 wherein the step of acquiring images comprises capturing
20 images using a microlens array positioned in front of a fiber bundle so as to limit acceptance angle, thereby increasing the rejection of scattered light .
22. The method of claim 1 wherein the step of acquiring images comprises capturing images using a coherent fiber bundle attached to a detector pixel array.
23. The method of claim 1, wherein the specimen region comprises a specimen that has
25 been pressure-injected into a micro-capillary tube.
24. A process for presenting a specimen to an optical imaging system, comprising the steps of:
 - a) containing a specimen mounted on an optically clear solid substrate within an optically clear micro-capillary tube;

b) pressing the micro-capillary tube between two solid sheets of material, such that the lateral motion of said capillary is constrained by said sheets of material;

c) immersing the micro-capillary tube in an index-matching material; and

5 d) allowing the micro-capillary tube to be rotated about its axis.

25. The process of claim 24, wherein the index-matching material comprises an optical oil with an index of refraction substantially matched to the index of refraction of the micro-capillary tube.

10 26. The process of claim 24, wherein the micro-capillary tube contains a suspending medium having an index of refraction substantially matched to the index of refraction of the micro-capillary tube.

27. The process of claim 24, wherein a solid, optically clear sheet of material is fixed to constrain the micro-capillary tube's motion in a direction perpendicular to a planar surface of the substrate.

15 28. A method for multi-dimensional imaging of a specimen region, comprising the steps of:

a) arranging at least two sets of illumination and image capturing systems in an arc about a specimen region;

20 b) operating each set of illumination and image capturing systems to capture images from a continuum of parallel focal planes, where each of the continuum of parallel focal planes is within the specimen region and is substantially perpendicular to the incident light rays from one of said illumination and image capturing systems, such that a pseudo-projection is simultaneously compiled from each of said illumination and image capturing systems; and

25 c) step b) is repeated for one or more viewpoints about an arc at least partially encircling the specimen region, suitable for tomographic image reconstruction.

29. A system for shadowgram formation for optical tomography comprising:

a piezoelectric transducer;

an objective lens coupled to the piezoelectric transducer;

30 a computer-controlled light source and condenser lens assembly;

a specimen assembly coupled to a means for translation relatively to the objective lens;

a micro-capillary tube containing a specimen;

a rotational stage coupled to rotate the micro-capillary tube;

5 a video camera disposed to receive photons from the objective lens; and

a computer linked to control the piezoelectric transducer, the computer-controlled light source and condenser lens assembly and the rotational stage, and coupled to receive images from the video camera where the piezoelectric transducer axially moves the objective lens to scan a continuum of focal planes in the specimen during a single integration cycle of the video camera.

30. The system of claim 29 wherein the specimen assembly comprises a microscope slide having a plurality of cover slips; and a micro-capillary tube captured within the microscope slide where index matching material provides a uniform medium between the micro-capillary tube and the cover slips so as to reducing optical aberrations.

15 31. The system of claim 30 wherein the index matching material comprises material selected from the group consisting of optical gels, oils, fluids, polymer and epoxy.

32. The system of claim 29 wherein the specimen assembly includes a specimen held in a medium selected from the group consisting of index-matching epoxy, embedding media, plastic polymer, index-matching gels and index-matching viscous fluids.

20 33. The system of claim 29 wherein the specimen assembly includes a specimen injected within a viscous index-matched fluid or gel into a micro-capillary tube using positive pressure.

34. The system of claim 29 wherein the specimen comprises a biological specimen stained with at least one of absorptive dyes, absorbing and light scattering dyes, antibody labels, antibodies conjugated with metal particles, quantum dots, plastic micro-spheres, fluorescent labels.

25 35. The system of claim 29 wherein the computer-controlled condenser and light source comprises an illumination source selected from the group consisting of at least one incandescent bulb, an arc lamp, a laser, a point source, a virtual point source and a light emitting diode.

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36. The system of claim 29 wherein the piezoelectric transducer moves the objective lens in response to a pre-selected waveform.

37. The system of claim 36 wherein the pre-selected waveform comprises a waveform selected from the group consisting of a geometric waveform, ramp waveform, and a sinusoidal waveform.

38. An optical tomography system employing multiple sets of pseudo-projection viewing subsystems, where a video camera captures multiple perspectives in parallel from the same specimen, the system comprising:

at least two optical imaging systems, each optical imaging system including a light source, a piezoelectric element, an objective lens, and a detector array disposed to acquire images specimen from a different viewpoint;

a specimen within a medium having a predetermined index of refraction captured; and

where the two or more optical imaging systems are arranged about a central axis of the specimen at regular intervals and where the piezoelectric element axially moves the objective lens to scan a continuum of focal planes in the specimen during a single integration cycle of the video camera.

39. The optical tomography system of claim 38 where the specimen is held within a micro-capillary tube.

40. An optical tomography system employing multiple sets of pseudo-projection viewing subsystems, the system comprising:

a series of specimens carried by a rigid medium, where the rigid medium includes one or more fiducials for registration;

where each of the multiple sets of pseudo-projection viewing subsystems include an image detector, disposed to receive image information from an objective lens, illuminated by an illumination system; and

a translation element for moving the objective lens with respect to the specimen to scan the focal plane continuously and where images are summed optically at the detector.

41. The system of claim 40 where the rigid medium comprises a selected one of a micro-capillary tube and a polymer optical fiber.

42. The system of claim 40 where each fiducial is used with conventional automatic image registration techniques on the images being integrated on the image detector, on individual images that are being summed for a single integration by the computer, and the registration of the multiple pseudo-projections as the rigid medium is rotated.

5 43. The system of claim 40 where identifying indicia are located proximate each specimen.

44. A method for reducing scatter in an optical system comprising the steps of illuminating a region of interest with a light source, capturing radiation emanating from the region of interest using an array of collimator fibers, and mapping each fiber to a
10 single pixel on a photosensor array with an arrangement of collimators that have a limited acceptance angle so that a portion of scattered light is rejected.

45. The method of claim 44 wherein the light source is a virtual point source.

46. The method of claim 44 wherein the photosensor array comprises a CCD array.

47. The method of claim 44 wherein a microlens array is positioned in front of the array
15 of collimator fibers so as to limit acceptance angle, thereby increasing the rejection of scattered light .

48. The system of claim 45 wherein the virtual point-source comprises two or more probes joined to the region of interest.

50. An optical tomography system comprising:

20 a matching objective lens system, including a pair of objective lenses and actuators symmetrically placed on both sides of an object of interest within a micro-capillary tube where the total optical path difference is defined as the net sum of the index of refraction multiplied by the difference in length of the optical ray along the total ray path, where one of the objective lenses is illuminated to function as an illuminating
25 lens passing illuminating light beams and the second serves as a collecting objective lens transmitting collecting light beams;

wherein a plurality of two-dimensional image slices of the object of interest is obtained by scanning both the illuminating light beams by one or two scanning mirrors and the collecting light beams by one or two descanning mirrors in synchrony so that the
30 confocal arrangement stays in optical alignment; and

wherein a three-dimensional image is assembled by capturing the plurality of two-dimensional image slices along the optical axis and a new image slice is generated by changing the plane of focus of the two objective lenses in synchrony, stepping the axial position of the two objective lens assemblies with respect to the capillary tube, or
5 adjusting the capillary tube position along the optical axis.

51. The system of claim 50 wherein the micro-capillary tube is rotated to generate a second three-dimensional view of the cell that is used to compensate for the non-symmetric point spread function of the objective lens, producing lower axial resolution than lateral resolution.

10 52. The system of claim 50 wherein illuminating light beams and the collecting light beams comprise one-dimensional or two-dimensional arrays of light beams.

53. The system of claim 50 wherein illuminating light beams and their point sources are conjugate to a camera and a software system to create a one-dimensional or two-dimensional array of virtual spatial filters which eliminates the need for one or more
15 descanning mirrors.

54. The method of claim 1 further including the step of separating acquired images based on color to produce two or more images, with one image primarily consisting of features generated by absorption by a dye/marker.

55. The method of claim 1 wherein the step of acquiring images further includes the step
20 of separating color in the specimen region to produce two or more images, with one image primarily consisting of features generated by absorption by a dye/marker.